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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/216,538	03/23/94	GOELET	P 637103CIP

SISSON, B EXAMINER

18N2/0605

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ART UNIT	PAPER NUMBER
1807	9

DATE MAILED: 06/05/95

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☑ Responsive to communication filed on 4-6-95 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), ___ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☑ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☑ Claims 30 - 46 are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☑ Claims 1 - 29 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☑ Claims 30 - 46 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev. 9-89)

Part III DETAILED ACTION

Re. Restriction requirement

Applicant's election with traverse of Group V, claims 30 and 31, in Paper No. 8, received 06 April 1995, is acknowledged. The traversal is on the ground(s) that the inventions of Groups II, III, IV, and V are not distinct, one from the other, due to their concordance of class and subclass. Said traversal is found to be moot as all originally filed claims have been cancelled and the new claims are all drawn to the elected invention.

Rejection under 35 U.S.C. 112, second paragraph

Claims 31 and 33-44 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 31 is indefinite with respect to just what constitutes "genetic bit analysis" and what one is "interrogating" for. Claims 33-44 which depend from said claim 31 fail to overcome this issue of indefiniteness and are similarly indefinite.

Rejection under 35 U.S.C. 103

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary

skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 30-38 and 42-46 are rejected under 35 U.S.C. § 103 as being unpatentable over Reiss et al., (REISS) in view of and Wheeler et al., (WHEELER).

REISS provides a review of the advancements of polymerase chain reaction (PCR) in the detection of numerous diseases in humans. Table 1 (p. 2) provides a listing a inherited diseases that have been diagnosed by PCR-based methodologies. The use of amplification methodologies, e.g., PCR, has been found to be highly effective in the diagnosis of sickle cell anemia; sickle cell anemia is due to a point mutation in an allele. While REISS does not teach specifically of the determination of the normal nucleotide residue sequence of the human individual, it is evident that in order for one to diagnose a point mutation, one must first know what the normal sequence is, develop primers that would allow for the amplification of the target sequence.

REISS does not teach of the type of control used.

WHEELER (p. 1800, right col., third par.) teaches of a variety of controls that were used for the amplification study, including the use of positive and negative controls (applicant's

"reference" samples). While the source of the DNA in the study performed by WHEELER was derived from a porcine rather than a human source, such is not considered significant as the material being amplified was still a nucleic acid.

In view of the showing of the prior art of record, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have applied the concept of using positive and negative controls as taught by WHEELER in the application of detecting point mutations and restriction fragment polymorphisms (RFLPs) in humans which are correlated with various diseases as taught by REISS. In view of the numerous diseases which have been diagnosed in humans as a result of PCR-based methodologies, said artisan would have had a reasonable expectation of success in the detection and diagnosis of such very diseases.

Claim 39 is rejected under 35 U.S.C. § 103 as being unpatentable over REISS in view of WHEELER as applied to claims 30-38 and 42-46 above, and further in view of GOELET et al., (GOELET)

GOELET (p. 37, last par., bridging to p. 38, first par.) teaches the use of dideoxynucleotides in primer extension reactions. This meets a limitation of claim 39.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have applied the use of dideoxynucleotides in primer extension reactions as taught by GOELET in the method of detecting a polymorphic region of a nucleic acid derived from a human as taught by REISS as such would afford the artisan with the capacity to readily detect the presence or absence of a suspected point mutation which can be indicative of an inheritable

disease. Given that the ability to incorporate ddNTPs into a primer extension product was well known in the art as well as the use of controls or reference samples in amplification reactions, and given the wide applicability of amplification-based methods for the detection of numerous diseases in humans, said artisan would have had a reasonable expectation of success.

Claims 40 and 41 are rejected under 35 U.S.C. § 103 as being unpatentable over REISS in view of WHEELER and GOELET as applied to claims 30-39 and 42-46 above, and further in view of Urdea.

Urdea (col. 3, first par.) teaches the use of a solid support which has attached thereto an oligonucleotide that in turn captures a target nucleic acid that is subsequently used in a primer extension reaction. It is taught that the "analyte polynucleotide" may be optionally removed from the support for the amplification reaction. Such a showing clearly indicates that amplification of a target nucleic acid while the target nucleic acid is immobilized to a support is achievable. This meets a limitation of claims 40 and 41.

In view of the showing of the prior art of record, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have applied the principles of immobilizing a target nucleic acid to a support and subsequently amplifying same as taught by Urdea while using dideoxynucleotides in said primer extension reaction as taught by GOELET, even to the exclusion of other dNTPs (see p. 38, first par, where it is taught that only one nucleotide, a dideoxynucleotide, is added to one primer) so as to allow for the detection of

polymorphisms in DNA from humans as taught by REISS and using the controls as taught by WHEELER.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (703) 308-3978. The examiner can normally be reached on Monday through Thursday from 6:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Art Unit is (703) 305-7939.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

B. L. Sisson

Bradley L. Sisson
Assistant Examiner

May 24, 1995

W. GARY JONES
SUPERVISORY PATENT EXAMINER
GROUP 1800
5/30/95